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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/258,132	02/26/99	GOELET	04990.0007.U

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EXAMINER
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ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 05/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.  
09/258,132

Applicant(s)  
Goelet et al.

Examiner  
Lisa Athur

Art Unit  
1655



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1) ☒ Responsive to communication(s) filed on Feb 28, 2001

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

## Disposition of Claims

4) ☒ Claim(s) 60-63 is/are pending in the application.

4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☒ Claim(s) 60-63 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirements.

## Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some\* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10

20) ☐ Other

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1. This action is in response to the paper filed February 28, 2001 in which claims 60-63 have been amended. All of the amendments and arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is FINAL.

**MAINTAINED REJECTIONS**

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 60-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 60-63 are directed to a method in which either one or more unique oligonucleotide primers are attached to a unique affinity moiety which specifically binds to a discrete position on a solid support or a plurality of unique oligonucleotide primers are attached to discrete positions of a solid support and then the target nucleic acid is added and to form a duplex and extension occurs on the immobilized primers. Additionally, claim 63 further includes a step of sorting the extended primers by affinity capture. None of these concepts have been disclosed in the specification. The preliminary amendment point to page 27, lines 12-24, pages 29 and 30 and page 31, lines 25-35 as providing support for these the new claims. However, upon thorough

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review of specification, particularly the cited portions of the specification, the claimed subject matter was found to be insufficiently described to reasonably convey to the skilled artisan that applicant was in possession of the claimed invention at the time of filing. While the specification described attaching one or more affinity moieties to the primers to permit affinity separation (page 27, lines 12-24), and described the affinity moiety as being a complementary nucleic acid sequence (page 27, lines 19-24), the specification does not describe the concept of attaching the primers or the affinity moieties to discrete positions on a solid support. From the specification it is clear that the intent of the immobilization on the solid support and the attachment of affinity moieties is to achieve separation of the extended primer from the unincorporated labeled terminators. Page 29, line 31 through page 30, line 3, teach the concept of simultaneous analysis of more than one oligonucleotide using more than one affinity group. This teaching, however, is not equivalent to the attachment of a plurality of oligonucleotide primers or a plurality of affinity moieties to "discrete positions" of a solid support. This concept of "discrete positions" has not been described in the specification and does not appear to have been part of the original inventive concept. The claims, as written, read on methods using oligonucleotide array technology which was not described in the specification. The specification only teaches the general concept that multiple oligonucleotide primers each with a different affinity moiety can be used to detect multiple target nucleotides. However, the specification does not teach the more complex concept of specifically arranging the oligonucleotides and/or affinity moieties to discrete positions on a solid support and determining the identity of a target nucleotide by determining its position on a

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solid support. Claim 63 is particularly unsupported by the specification because the specification contains no description of sorting the extended primers by affinity capture and then determining the identity and location of the terminator to determine the identity of the bases at a plurality of sites. These concepts are unobvious extensions of the teachings that a different affinity moiety can be used to capture a plurality of different primers because the teachings contain no reference using the affinity moieties to sort the primers or to capture the primers at specific locations on a solid support as a means for identification of the target bases. Therefore, for the reasons, given above, the claims introduce new matter into the specification.

***Response to Arguments***

The response traverses the rejection on the grounds that the specification supports the claims, especially at page 31, lines 23-35. The response also argues that support for the binding of oligonucleotides to discrete positions necessarily follows from the teaching of using more than one affinity reagent to analyze more than one oligonucleotide and the teaching that by combining the use of four differently labeled terminators with the use of many primers or templates tagged with different groups, many different nucleic acid sequences can be typed simultaneously. Finally, the response asserts that these teachings in the specification imply the concept of sorting the extended primers by affinity capture.

All of these arguments have been considered but are deemed non-persuasive for the following reasons. The argument that the concept of discrete or defined positions is implied by the teaching of using different affinity moieties on different primers is not convincing because

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discrete and defined positions means a specific and known location. The specification does not teach the concept of immobilizing a particular affinity moiety at a specific position on the solid support and nowhere teaches using that specific location to identify the nucleotide via a label on the specific base which is added at the 3' of the primer. Instead, the specification teaches identification of the added base by identification of the label only or by the presence of the label on a solid support but not at a specific position on the solid support. At page 26, lines 11-27, the specification describes the use of affinity moieties attached to the nucleic acid of interest that permit separation of the nucleic acid of interest from unincorporated reagent and/or primer. At page 27, lines 12-24, the specification describes the use of affinity moieties attached to the primers to permit the separation from unincorporated reagent and/or nucleic acid of interest and the specification specifically teaches that the affinity moiety can be a nucleic acid which is attached to a solid support. The specification does describe the application of the method to identifying the nucleotide at multiple positions using a different primer for each position. However, nowhere in the specification is there a description of the attachment of these nucleic acid affinity moieties to defined positions such that the identity of the nucleotide base can be determined by determining its location on a solid support as opposed determining the identity of the label. The specification also contains no description of any sort of a sorting step. These concepts are not implied from the teachings in the specification because the specification teaches the use of the solid support for the purpose of simplifying the separation of the target to be detected from the unincorporated reagents. The skilled artisan would not immediately envisage sorting multiple targets and

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identifying specific bases based upon their location on a solid support. At the time of filing array technology was not being generally applied to nucleic acid detection methods. Therefore, for these reasons the rejection is maintained.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 60-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 60-63 are indefinite over the recitation of the terms “discrete position” and “defined positions” because the terms make the claims unclear as to whether the each primer or affinity moiety is attached at a specific and unique location on a solid support or whether a discrete position includes a spot in a dot blot, for example, as shown in figure 8, wherein the dot blot contains the entire reaction mixture.

***Response to arguments***

The response argues that discrete and defined positions are defined in the specification and that dot blots are one example of a solid support and that solid support is defined in the specification.

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This argument has been thoroughly reviewed but is not convincing because <sup>with</sup> a dot blot is an example of a solid support it is not a definition of "discrete" or "defined" position as it applies to a location of a primer or target nucleic acid of interest or a label. The meaning of these terms is critical to determine the metes and bounds of these claims as encompassing only Southern type hybridization analysis versus hybridization using array technology. Therefore, this rejection is maintained.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 60-63 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-56 of U.S. Patent No. 6,004,744.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they contain overlapping subject matter. Claims 60-63 encompass embodiments using one immobilized oligonucleotide primer for the single base extension reaction to identify a specific nucleotide. Claims 13-56 of patent 6,004,744 are also drawn to methods using an immobilized



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primer for the single base extension reaction. The recitation in claims 60-63 that the primer is immobilized in a “discrete” or “defined” position is unclear (see rejection made above under 35 U.S.C. 112, second paragraph), but does not differentiate the instantly claimed methods from that of patent 6,004,744, particularly for the embodiments wherein only one primer is immobilized.

8. Claims 60-63 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-48 of U.S. Patent No. 5,888,819 in view of Dattagupta et al.

The claims of patent 5,888,819 are drawn to a method for determining a the base at a specific position in a nucleic acid by performing a single base primer extension reaction in the presence of labeled terminators and the absence of dNTPs. The claims do not include a limitation that the primers are immobilized on a solid support. However, Dattagupta et al. teach that primer extension reactions can be performed on immobilized primers with the advantage being that unincorporated nucleotides can be easily separated from the extension product. Therefore, it would have been prima facie obvious to one of ordinary skill to have modified the method of the claims in patent 5,888,819 to be immobilized as taught by Dattagupta et al. In order to achieve the expected benefit of more easily and quickly removing unincorporated nucleotides from the primer extension reaction. Applicant should note that this rejection is directed to the embodiments of the claims limited to use of a single primer.

***Response to Arguments***

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The response states that a terminal disclaimer was submitted. However, no terminal disclaimer has been received and therefore the rejection is maintained.

9. Claims 60-63 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-59 of copending Application No. 09/258,132 in view of Dattagupta et al.

The claims of application 09/258,132 are drawn to a method for determining a the base at a specific position in a nucleic acid by performing a single base primer extension reaction in the presence of labeled terminators. The claims do not include a limitation that the primers are immobilized on a solid support. However, Dattagupta et al. teach that primer extension reactions can be performed on immobilized primers with the advantage being that unincorporated nucleotides can be easily separated from the extension product. Therefore, it would have been prima facie obvious to one of ordinary skill to have modified the method of the claims in application 09/258,132 to be immobilized as taught by Dattagupta et al. In order to achieve the expected benefit of more easily and quickly removing unincorporated nucleotides from the primer extension reaction. Applicant should note that this rejection is directed to the embodiments of the claims limited to use of a single primer.

This is a provisional obviousness-type double patenting rejection.

***Response to Arguments***

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The response states that a terminal disclaimer was submitted. However, no terminal disclaimer has been received and therefore the rejection is maintained.

10. No claims are allowable.

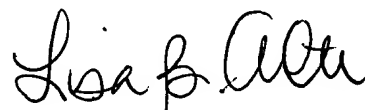
11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Monday-Thursday from 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



LISA B. ARTHUR  
PRIMARY EXAMINER  
GROUP 1800 | 600

May 14, 2001